

**REMARKS**

Claims 1-15 are pending in this application. Claim 1 has been amended hereby.

**Claims 1-15 stand rejected under 35 U.S.C. 102(b) as being anticipated by Green et al. (U.S. Patent No. 4,016,036).**

The rejection is overcome by the amendment to claim 1, which has been amended to further clarify the distinction between the present invention and Green et al.

Claim 1 has been amended to recite "so as to leave an extracellular matrix on a surface of said culture vessel". Support for this recitation may be found in the specification on page 3, lines 22-27, as well as page 5, line 16, and page 8, line 8.

Applicants assert that Green et al. does not disclose the recitation of claim 1. Green does state that "The presence of either fibroblast cells or fibroblast cell products, **which can be supplied from medium harvested from** fibroblast cultures, is essential to support growth of keratinocytes." (column 2, lines 38-41, emphasis added). However, Green does **not** disclose <sup>inherent in Green</sup> any use of an extracellular matrix left on the surface of the culture vessel in which the fibroblasts are irradiated.

Green also clearly implies that the fibroblast cell products are floating free in the medium and the reference does not suggest that any useful products are attached to the surface of a culture vessel. For example, in column 3, line 30, Green states:

"Actual contact with fibroblast cells is not necessary for growth and keratinization in all cases. It was found, for example, that XB clonal cells could be supported by mouse fibroblast 3T3 cells **located some distance away** in a culture dish. XB cells were also able to form colonies and keratinize in the absence of 3T3 cells if the **growth medium was previously conditioned** by 3T3 cells. Conditioning was achieved, for example, by exposing saturation density cultures of 3T3 cells to medium for 1 day. **The medium was then removed and filtered.**" (Emphasis added)

That is, Green is clearly teaching that a soluble component in the growth medium, not attached to the flask in which the 3T3 cells are grown, is the active component.

In Green's Example 2 in column 7, line 14, irradiated 3T3 cells are trypsinized and removed from the dish in which they were grown and irradiated. These 3T3 cells are inoculated with the XA1.2 cells, but there is **no** contact of the XA1.2 cells with the **dishes** in which the 3T3 cells were grown and irradiated. Therefore, any extracellular matrix that may be present on these dishes in Green is not used for growth of the XA1.2 cells.

The present claims clearly recite an invention not disclosed or suggested by Green. The amendment to claim 1 clarifies that in performing the method of the claims, an extracellular matrix is left on the surface of the culture dish, and the target cells therefore are grown in contact with this extracellular matrix. Green does not disclose nor suggest that the keratinocytes are grown in contact with an extracellular matrix that has adhered to the culture vessel in which the fibroblasts are grown.

Applicants therefore submit that claims 1-15, as amended, are not anticipated by Green et al. and, moreover, are non-obvious over Green et al.

A marked-up version showing the changes made by the present amendment is attached hereto as "Version with Markings to Show Changes Made."

If, for any reason, it is felt that this application is not now in condition for allowance, the Examiner is requested to contact Applicants undersigned Agent at the telephone number indicated below to arrange for an interview to expedite the disposition of this case.


Amendment Accompanying RCE  
Nobutaka YAMAMOTO et al.

U.S. Patent Application S.N. 09/718,388  
Attorney Docket No. 001554

In the event that this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. Please charge any fees for such an extension of time and any other fees which may be due with respect to this paper, to Deposit Account No. 01-2340.

Respectfully submitted,

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Enclosures: Version with Markings to Show Changes Made  
Request for Continued Examination  
Petition for Extension of Time

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

1. (Twice Amended) A method for adhering and proliferating target cells, which comprises the steps of:

inoculating, culturing and then killing, in a culture vessel, fibroblasts derived from a mammal, so as to leave an extracellular matrix on a surface of said culture vessel, and then culturing the target cells in said culture vessel.